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Original Research Article

Preoperative Levels of Serum Total Antioxidants and Sialic Acid in Leiomyoma: A Case Control Study

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Abstract

Background: The exact cause of leiomyoma which affects at least 5 million women throughout the world is not known. Currently there are only few markers for leiomyoma which includes serum protein, prolactin, CA 125, soluble serum HLA-G, vascular endothelial growth factor and lactate dehydrogenase etc. However a reliable marker is still not found. This study is undertaken to analyse the association of oxidative stress and sialic acid in leiomyoma patients compared with control group.

Methods: This non interventional cross sectional study comprised of 50 study subjects with 25 leiomyoma patients (case group) and 25 healthy individuals (control group). Total antioxidant was estimated by phosphomolybdenum method. Serum sialic acid was measured by using diphenylamine method.

Results: The result showed a significant increase in the sialic acid level in leiomyoma patients (80.51±9.61) in comparison with normal healthy individuals (57.73±7.77) with p=0.05. Also an insignificant correlation of Total antioxidant level [TAC] between case and control group (p= 0.591).

Conclusion: In conclusion, serum sialic acid concentration is significantly increased in leiomyoma patients as compared to healthy control. This suggests a probable clinical use of sialic acid evaluation in future as a marker of leiomyoma. An insignificant correlation between total antioxidant and leiomyoma can be due to less involvement of oxidative stress in the pathogenesis of leiomyoma.

Keywords: Leiomyoma; Sialic Acid; Total Antioxidants; Tumour Marker.

Introduction

Leiomyoma one of the most common benign gynaecological tumours of women in reproductive age group of 20-40 years accounts for significant morbidity and the most common reason for hysterectomy. Between 80% to 90% of African American women and 70% of white women develop fibroid by age of 50. In 2000, more than 2,50,000 hospital admissions were related to uterine fibroids. Every year fibroid leads to more than 2,00,000 hysterectomy [1-3]. Leiomyoma can occur in any organ but most commonly seen in the uterus. These are benign tumours clinically manifests with excessive menstrual bleeding, anaemia and infertility. Risk factors for this include early menarche, hypertension, obesity and uterine infections [1-3].

Histopathology of leiomyoma shows excessive smooth muscle cell proliferation, large amount of extracellular matrix deposition which is surrounded by a thin pseudo capsule of areolar tissue, containing feeding vessels [1].

The pathogenesis and aetiology of leiomyoma is not well understood. Its pathogenesis is multi factorial and the precise mechanism involved in its initiation and growth remains unclear. Several factors involved in the enlargement of leiomyoma, includes interaction between various genes, hormones, growth factors and cytokines although oestrogen and progesterone have been traditionally considered as the major promoter of leiomyoma growth [1,2].

An inadequate antioxidant protection or an excessive production of reactive oxygen species (ROS) can alter the cellular oxidative balance creating a condition known as oxidative stress. ROS have many physiological regulatory functions and are also implicated in development of a wide spectrum of diseases [2,3].

The mammalian cell has an adequate antioxidant system to cope with excessive ROS produced under normal physiological conditions. This system consist of antioxidant vitamins, thiol containing compounds such as reduced glutathione (GSH) and antioxidant enzymes, including superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx)and glutathione reductase (GR). Variations in antioxidant capacity may influence individual susceptibility to some diseases associated with deleterious effects of oxidative reactions [1-3].

Oestrogen as well as oestrogen metabolites has been reported to act as pro-oxidants. Estrogen induced ROS play an important role in cell transformation, cell proliferation, migration and invasion by increasing genomic instability and increased redox sensitive transcription factors [3,4].

Sialic acid is an N or O substituted derivative of neraminic acid, a monosaccharide with nine carbon backbone. These are entered in circulation by cell lysis and are having considerable interest because of their potential diagnostic value. The dramatic changes in glycolipid composition and metabolism associated with oncogenic transformation suggest a specific role for membrane glycolipids in regulation of cell growth and cellular interaction [5,6].

In tissue, deletion of complex glycolipids due to a block in synthesis and the synthesis of new glycolipid due to activation of normally unexpressed glycosyl transferase produce tumour distinctive glycolipids, which are tumour associated antigens or markers [5,6].

There are very few studies suggesting any correlation between antioxidant status and sialic acid in patients with leiomyoma in the world and Indian literature.

The rationale behind our study is to estimate the TAC and sialic acid in patients with leiomyoma and compare it with control normal healthy individuals.

Aims and Objectives

To access the preoperative serum levels of total antioxidants and sialic acid in patients with leiomyoma (case group) compared with control group.

Materials and Methods

This was a cross sectional case-control study done in tertiary hospital located in Dakshina Kannada district. After obtaining approval from the institutional ethical committee, written consent was taken from both case and control groups.

Sample Size: 50 subjects were included (25 controls +25 cases)

Control Group: 25 samples collected from women without any evidence of leiomyoma.

Case group: 25 patients admitted with various symptoms that were histopathologically confirmed to have leiomyoma.

Inclusion Criteria

Patients belonging to the age group 20-40 years who are histologically proven to have uterine leiomyoma.

Exclusion Criteria

1. Patients with malignancy and borderline tumours
2. Diabetes mellitus, chronic diseases, hypertension
3. Hepatitis B and C, Human Immunodeficiency Virus infection

Blood samples were collected in appropriate vacutainers after taking informed consent. Serum was separated by centrifugation at 3000rpm for 15 minutes, stored at -20 degree Celsius and analyzed for serum TAC and Sialic acid levels. The data thus obtained was compiled and analyzed using SPSS software.

Results

The study involved estimation of TAC and sialic acid levels in leiomyoma patients as well as in healthy individuals.

Mean age of control group was 31.6 years whereas the mean age of case group was 33.5 years.

*No significant correlation was found using Unpaired t-test for TAC values between cases and control(p value:0.5866, with degrees of freedom:49).

Significant correlation was found using Unpaired t-test for Sialic acid levels between cases and control(p value<0.0001, with degrees of freedom:49).

Two- tailed Pearson correlation done between TAC and Sialic acid levels of the control group showed a significant positive correlation(correlation = 0.426; p=0.03).

The same in the case group showed a negative correlation, which statistically is insignificant.

The study showed an increase in sialic acid level in leiomyoma patients (80.51±9.61mg/dl) in comparison with normal healthy individuals (57.73±7.77mg/dl) with p value of < 0.05.

This study showed no significant difference in TAC between case and control group (p= 0.591).

Table 1: Comparison between values of TAC and Sialic acid between cases and controls

	TAC(mM/L)			Sialic acid(mg/dL)		
	Maximum value	Mean	Standard Deviation	Maximum value	Mean	Standard Deviation
Cases	1.01	0.7548*	0.14176	108.8	80.5120#	9.61676
Controls	1.17	0.7823*	0.20916	69.6	57.7354#	7.77698

Discussion

The exact cause of leiomyoma which affects at least 5 million women throughout the world is not known. Currently there are only few markers for leiomyoma which includes serum protein, prolactin, CA 125 soluble serum HLA-G, vascular endothelial growth factor and lactate dehydrogenase etc. However a reliable marker is still not found. In our study of 50 subjects, 25 leiomyoma patients and 25 normal healthy individuals of 20-40 years age group were included. Serum total antioxidant and sialic acid was estimated among this group [2,4,6,7].

Sialic acid in control was found to be 57.73±7.77 mg/dl and in case was found to be 80.51±9.61 mg/dl. It was observed that serum sialic acid was significantly increased in case than in control.

According to a previous study conducted by G Rajeshwari et al, sialic acid is a common terminal sugar unit of oligosaccharides of glycoproteins and glycolipids which are cell surface constituents. These enter into circulation by shedding of from cell. The changes in glycolipid composition and the metabolism associated with tumour suggest a specific role for membrane glycolipid in regulation of cell growth and cellular interaction. The two types of changes, one the deletion of complex glycolipids due to block in synthesis, which lead to accumulation of precursor structure and the second synthesis of new glycolipid due to activation of normally unexpressed glycosyl transferases can produce tumour distinctive glycolipids some of which are tumour associated antigen or marker [5,7,8,9] . Sialic acid is used as tumour marker in oral, gastric and other cancers. But also its elevation in non neoplastic lesions makes it non specific tumour marker [1-8].

Another study conducted by kennedy [9] shows an effect of oestrogen and progesterone on sialic acid. The study shows that both oestrogen and progesterone act synergistically to increase the concentration of sialic acid. However in our study, we could not do the oestrogen and progesterone assay, hence such association was not established.

TAC in control group was found to be 0.78±0.209 Mm/L and in the case group it was found to be 0.754 ± 0.14 Mm/L. A negative trend that is statistically insignificant was observed for TAC in case and control group. Previous studies Santulli P [1] which have arrived at a conclusion that there is a significant positive correlation between total antioxidant and leiomyoma have attributed this to the oxidative stress but since in our study we have not observed such change. We would propose that oxidative is not of much significance in the pathogenesis of leiomyoma. However this could possibly be due to the limiting factors like the small sample size which might not be statistically significant enough to arrive at a definitive conclusion regarding their relation. So further and more studies on a larger scale is required to arrive at a conclusion as to whether the levels of antioxidant relates to leiomyoma.

Conclusion

In conclusion, the present study suggests that serum sialic acid concentration is significantly increased in leiomyoma patients as compared to healthy control. From this study, we arrive at a conclusion that increase in sialic acid in leiomyoma is may be related to the inflammatory response produced or due to increase in levels of oestrogen and progesterone(as leiomyoma usually associated in increased oestrogen and progesterone). This suggests a probable clinical use of sialic acid evaluation in future as a marker of leiomyoma. We also arrive at an insignificant correlation between total antioxidant and leiomyoma which can be due to relative less involvement of oxidative stress in the pathogenesis of leiomyoma.

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